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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,561	03/01/2007	Howard J. Federoff	176/62732 (6-1275)	7894

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EXAMINER	
KELLY, ROBERT M	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
07/30/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,561	FEDEROFF ET AL.	
	Examiner	Art Unit	
	ROBERT M. KELLY	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-7,9,12,16-20,22-26,28-31,33 and 34* is/are pending in the application.

4a) Of the above claim(s) *1,2,4-7,9,12,16-20 and 22-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-31,33 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :5/4/06; 3/14/08; 6/23/08; 9/10/08; 10/14/08; 7/9/09.

DETAILED ACTION

Applicant's response to restriction requirement of 7/9/09 is entered.

Claims 1, 2, 4-7, 9, 12, 16-20, 22-26, 28-31, 33, and 34 are presently pending.

Election/Restrictions

Applicant's election without traverse of Group IV, drawn to treatments by administration of a nucleic acid encoding ABeta proteins in the reply filed on 4/17/09 is acknowledged.

Claims 1, 2, 4-7, 9, 12, 16-20, 22-26 are withdrawn, as being drawn to non-elected inventions.

Claims 28-31 and 33-34 are presently considered.

Claim Rejections - 35 USC § 112 - clarity

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 28 recites "wherein the transgene". Such lacks proper antecedent basis. To wit, does this refer to the "heterologous transgene", the encoded HSV genes, the encoded accessory protein, or something else?

Claim 30 recites "the transgene", in Claim 28. Such lacks proper antecedent basis. To wit, does this refer to the "heterologous transgene", the encoded HSV genes, the encoded accessory protein, or something else?

Claim 31 recites "the molecular adjuvant", in Claim 28. Such lacks antecedent basis.

Claims 33 and 34 each recite "the transgene" in Claim 28. Such lacks proper antecedent basis. To wit, does this refer to the "heterologous transgene", the encoded HSV genes, the encoded accessory protein, or something else?

Claims 29-31, 33, and 34 are rejected for depending from a rejected base claim and not overcoming the lack of clarity in such base claim.

Claim Rejections - 35 USC § 112 - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-31, 33, and 34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant's claims encompass methods of treatment of any form of neurodegenerative disease in a patient. The methods encompass (i) any administration of an HSV amplicon encoding the HSV origin of replication, cleavage, and packaging signals, and any heterologous transgene; (ii) any administration of vector(s) which encode all essential HSV genes, but lacking

packaging and cleavage signals, and such genes may be encoded in parts across several vectors; and (iii) administration of any vector encoding any accessory protein. Specifically encompassed diseases include spinal cord injury (p. 30), and specifically claimed diseases are Alzheimer's disease (Claim 29). The heterologous transgene may be any molecular adjuvant (Claim 30), or specifically tetanus toxin Fragment C (Claim 31). The heterologous transgene may also be any Abeta (Claim 33), or any Abeta and any molecular adjuvant (Claim 34).

Further, the only described neurodegenerative diseases are those of spinal cord damage, and Alzheimer's disease (e.g., p. 30, paragraph 3).

The specification provides no direction and/or guidance per se, to perform the method, such that the Artisan could reasonably predict it would work. Instead, only literal support is found for the claimed methods in the specification (e.g., p. 8, paragraph 1). Moreover, the specification teaches that increased exposures to amplicon vectors leads to death, probably due to encephalitis (inflammation of the brain associated with a viral infection) (p. 15, paragraph 2).

The Examples demonstrate only administrations of amplicons, without helper virus, and single administrations, which provide for the development of antibodies. Even the prophetic example fails to imagine a treatment with the co-adminstration of helper virus (p. 44), and this example does not even amount to a thought experiment that could be utilized to confirm the efficacy of treatment with amplicon alone, much less in the presence of the helper vectors.

The Art demonstrates, however, that immunization against Abeta proteins for antibodies which provide for treatment of the core embodiment, Alzheimer's disease (e.g., U.S. Patent No. 7,014,855 to Schenk, claims and paragraph 9 in the section entitled "III. Therapeutic Agents", subsection entitled "1. Alzheimer's Disease", where alternative delivery by, e.g., HSV vectors is

provided; U.S. Patent No. 6,972,127, to Schenk, Claims 1 and 4 and paragraph 9 in the section entitled "III. Therapeutic Agents", subsection entitled "1. Alzheimer's Disease", where alternative delivery by, e.g., HSV vectors is provided). Morever, because the claimed "regime[s]" claimed encompass the specifically taught delivery by HSV vector (as noted in the citation), it must also be enabled for such deliveries. Hence, the administration of such amplicons appears to be reasonably predictable to produce an immune response. Moreover, the use of fusions to tetanus toxoid and keyhold limpet hemocyanin appears enabled (e.g., U.S. Patent No. 6,946,135 to Schenk, claims and section entitled "III. Therapeutic Agents", subsection entitled "1. Alzheimer's Disease", sub-subsection entitled "3. Carrier Proteins"). Other patents demonstrating enablement for similar therapies as well as antibody therapy are U.S. Patents 6,946,135; 6,913,745; 6,905,686; 6,875,434; 6,866,850; 6,866,849; 6,787,523; 6,787,144; 6,787,143; 6,787,140; 6,787,139; 6,787,138; 6,761,888; and 6,743,427, all to Schenk. It is noted that several other related patents have been issued to Schenk, but involve related subject matter like transgenic animals and detection methods. Hence, it is hard to say that the methods would not induce an immune response which would eventually alleviate symptoms of the core embodiment, Alzheimer's disease, as well as amyloid plaque related diseases, as is shown in Schenk's claims.

On the other hand, Applicant's methods require administration of the amplicon and the other helper viruses into the subject. It has long been known that the object to administration of defective viruses is two fold: (i) to make space to add transgenes, and (ii) to avoid continuing infection. It is repeatedly noted in the Art that it is not safe to administer live, productive, herpes simplex virus (e.g., Herrlinger, et al. (2000) Human Gene Therapy, 11(10): 1429-38,

ABSTRACT). In this, it is recognized that the problem with replicative viruses, which in the present case are amplicons reproducing and infecting new cells, there is danger of toxicity, and specifically, encephalitis, as Applicant has demonstrated for subsequent infections with their amplicons (specification, p. 8, as shown above). For example, Kristensson, et al. (1978) Journal of the Neurological Science, 35(2-3): 331-40 (ABSTRACT ONLY), discusses that subcutaneous and cornea injections of HSV which can replicate can cause extensive destruction of the neural tissue (ABSTRACT). Further, intracerebral injection of virus causes meningitis (e.g., Thomas, et al. (2001) Journal of Neurovirology, 7(2): 105-16 (ABSTRACT ONLY)). Lastly, the subcutaneous injection of HSV causes death in animals (e.g., Davis, et al. (1978) Antimicrobial Agents and Chemotherapy, 14(5): 743-48, whole article).

From this, the Artisan would immediately realize that the uncontrolled formation of viral particles would likely cause infection of the brain and encephalitis. Still further, compounding on the discussion by Applicant that subsequent injections of viral amplicons caused death, likely by encephalitis, the Artisan would necessarily find it not reasonably predictable that any therapeutic effect would be seen prior to the death of the subject being treated.

Hence, the Artisan, despite being highly educated, would have to experiment to determine if such administrations would produce any therapeutic effect prior to the death of the animal. Such experimentation is considered undue as it would be the experimentation required to reasonably enable Applicant's claimed invention.

Therefore, the claims are not enabled.

Conclusion

No claim is allowed.Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT M. KELLY whose telephone number is (571)272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert M Kelly/
Primary Examiner, Art Unit 1633